



# United States Patent [19]

Domb et al.

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[54] **NANOPARTICLES AND MICROPARTICLES  
OF NON-LINEAR  
HYDROPHILIC-HYDROPHOBIC  
MULTIBLOCK COPOLYMERS**

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[57] **ABSTRACT**

Particles are provided that are not rapidly cleared from the blood stream by the macrophages of the reticuloendothelial system, and that can be modified to achieve variable release rates or to target specific cells or organs. The particles have a core of a multiblock copolymer formed by covalently linking a multifunctional compound with one or more hydrophobic polymers and one or more hydrophilic polymers, and contain a biologically active material. The terminal hydroxyl group of the poly(alkylene glycol) can be used to covalently attach onto the surface of the particles biologically active molecules, including antibodies targeted to specific cells or organs, or molecules affecting the charge, lipophilicity or hydrophilicity of the particle. The surface of the particle can also be modified by attaching biodegradable polymers of the same structure as those forming the core of the particles. The typical size of the particles is between 180 nm and 10,000 nm, preferably between 180 nm and 240 nm, although microparticles can also be formed as described herein. The particles can include magnetic particles or radiopaque materials for diagnostic imaging, biologically active molecules to be delivered to a site, or compounds for targeting the particles. The particles have a prolonged half-life in the blood compared to particles not containing poly(alkylene glycol) moieties on the surface.

**38 Claims, 7 Drawing Sheets**